Diagnosis and treatment of epididymal tuberculosis: A review of 47 cases

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Objective: To analyze the clinical manifestations,diagnosis,and treatment outcomes in a series of patients with epididymal tuberculosis.

Methods: This study is a retrospective data analysis of 47 cases of histologically-confirmed epididymal tuberculosis in patients treated at our hospital from November 2014 to December 2018.

Results: The average age of the patients was approximately 41.98 years.The epididymal lesion location was left-sided in 15 patients(31.9%),right-sided in 22 patients (46.8%),and bilateral in 10 patients (21.3%).The main symptoms were painless swelling of the scrotum in 21 cases (44.7%) and scrotal drop pain in 21 cases (44.7%). Scrotal physical examination revealed epididymal beaded enlargement in 12 patients (25.5%), testicular mass in 1 patient (2.1%), scrotal tenderness alone in 7 patients (14.9%), ill-defined epididymal-testicular border in 21 patients (44.7%), and sinus formation in 6 patients (12.8%). After 2 to 4 weeks of anti-tuberculosis chemotherapy, the patients underwent a surgical resection procedure. We found that 10 (83.3%) of the 12 patients whose main symptom was epididymal beaded enlargement underwent simple epididymal resection. Of the 21 patients whose main clinical manifestation was ill-defined testis-epididymis demarcation, 16 (72.2%) underwent epididymis-testicular resection. All patients underwent postoperative chemotherapy for 3 to 6 months. Postoperative follow-up showed good response to treatment.

Conclusion: It is difficult to diagnose early-stage epididymal tuberculosis. Epididymal tuberculosis is likely to have invaded surrounding tissues when signs such as epididymal beaded changes and ill-defined epididymis-testis border are present. Surgical resection combined with preoperative and postoperative chemotherapy is an effective approach to treating this condition.

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18 beaded enlargement in 12 patients (25.5%), testicular mass in 1 patient (2.1%), scrotal tenderness
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27 **Conclusion**:It is difficult to diagnose early-stage epididymal tuberculosis. Epididymal
28 tuberculosis is likely to have invaded surrounding tissues when signs such as epididymal beaded
29 changes and ill-defined epididymis-testis border are present.Surgical resection combined with
30 preoperative and postoperative chemotherapy is an effective approach to treating this condition.

31 **Keywords**:epididymal tuberculosis,clinical characteristics,chemotherapy

32

33 **Introduction:**Epididymal tuberculosis is a rare extrapulmonary form of tuberculosis that occurs
34 in young adults(Surati et al. 2012).Patients with this disease may have no obvious clinical
35 symptoms or only mild symptoms.The disease typically develops slowly and early diagnosis is
36 difficult;delayed diagnosis and misdiagnosis are common.Recently,due to the emergence of multi-
37 drug resistant bacteria (MDR), anti-tuberculosis drug resistance, and the widespread use of
38 glucocorticoids, the incidence of male genitourinary tuberculosis, including epididymal
39 tuberculosis, has been increasing worldwide. Epididymal tuberculosis remains an important health
40 problem in many developing countries,including China(Kulchavenya et al. 2012).The pathological
41 features of epididymal tuberculosis are extensive tissue destruction and fibrosis, eventually leading
42 to destruction of the epididymis and surrounding genital tissues and organs and complications such
43 as infertility and other serious effects on male reproductive system function.

44   At present, early diagnosis and regular chemotherapy are the keys to curing male reproductive
45 system tuberculosis and to avoid surgical treatment.However, due to its late onset and nonspecific
46 clinical signs and symptoms, and the lack of rapid, sensitive, and specific diagnostic methods,the
47 disease is often misdiagnosed or the diagnosis is delayed. Therefore, surgical treatment combined
48 with chemotherapy has been the preferred treatment approach to this disease. This study, a
49 retrospective analysis of a series of cases of epididymal tuberculosis, is intended to more fully
50 characterize the clinical features and outcomes of surgical treatment of this disease.

51 **Material and Methods:**We collected the medical records of 47 patients with histologically-
52 diagnosed epididymal tuberculosis from November 2012 to October 2018 at the Second Hospital
53 of Lanzhou University. Age, clinical signs and symptoms, diagnostic methods, and treatment
54 effects were collected from the patients' electronic medical records, and the final results were
55 compared and analyzed.The following information was supplied relating to ethical approvals (i.e.,
56 approving body and any reference numbers):Ethics Committee of Lanzhou University Second
57 Hospital Number:2019A-079.Written consent was obtained from all patients.

58 **Results:**The mean age of the patients was 41.98 years (range, 19-72 years); 15 patients (31.9%)
59 had tuberculosis in the left epididymis, 22 patients (46.8%) had tuberculosis in the right
60 epididymis, and 10 patients (21.3%) had bilateral epididymal tuberculosis. Of the 47 patients, 8
61 (17.0%) had a history of tuberculosis, including 3 cases of pulmonary tuberculosis, 4 cases of renal
62 tuberculosis, and 1 case of prostate tuberculosis(Table 1).

63   Main symptoms at the time of onset included: painless swelling of the scrotum in 21 patients
64 (44.7%); scrotal drop pain in 21 patients (44.7%); urinary tract irritation such as urinary frequency,
65 dysuria, and hematuria in 4 patients (8.5%); and scrotal skin ulceration in 1 patient (2.1%).
66 Systemic symptoms such as low-grade fever, fatigue, and night sweats occurred in 6 patients
67 (12.8%). All patients underwent scrotal physical examination, which revealed epididymal beaded

68 enlargement in 12 patients (25.5%), testicular mass in 1 patient (2.1%),scrotal tenderness alone in
69 7 patients (14.9%),ill-defined epididymal testicular border in 21 patients (44.7%), and sinus
70 formation in 6 patients (12.8%)(Table 1).

71 Urinalysis and chest imaging were performed in all patients.Twenty patients (42.6%) were
72 positive for white blood cells in urine and 8 patients (17.0%) were positive for red blood cells in
73 urine. Chest imaging was positive in 8 patients (17.0%). The preoperative diagnoses were
74 epididymal tuberculosis in 41 patients (87.2%), epididymal tumor in 3 patients (6.4%), and
75 epididymal mass in 3 patients (6.4%). All patients had evidence of surgical resection of the lesion.

76 Among the 47 cases, 41 (87.2%) were initially identified as epididymal tuberculosis and treated
77 pre-operatively with rifampicin, isoniazid, pyrazinamide, and ethambutol for 2 to 4 weeks.
78 Twenty-six patients (55.3%) had epididymectomy and 21 patients (44.7%) had epididymectomy
79 combined with orchiectomy, and all recovered well after surgery.

80 We found that 10 (83.3%) of the 12 patients whose main symptom was epididymal beaded
81 enlargement underwent simple epididymal resection and 2 (16.7%) underwent epididymis-
82 testicular resection.Of the 21 patients whose main clinical manifestation was ill-defined testis-
83 epididymis demarcation, 16 (72.2%) underwent epididymis-testicular resection and 5 epididymal
84 resection(Table 2).

85 Macroscopically, all specimens contained solitary or confluent pale, grayish caseous necrotic
86 nodules.Some lesions invaded the entire epididymis, some showed involvement of the testis with
87 adherence to the scrotum to form a cold abscess, and some showed the formation of ulcerated sinus
88 tracts in the skin. Microscopically, the centers of the specimens were red-stained with amorphous
89 granular, irregularly sized foci of caseous necrosis surrounded by tuberculous granulation tissue
90 (epithelioid cells, Langhans giant cells, and lymphocytes) (Figure 1,2).

91 All patients received anti-tuberculosis treatment with rifampicin, isoniazid, pyrazinamide, or
92 ethambutol after surgery for 3 to 6 months. No recurrence was reported.

93 **Discussion:**

94 The number of TB patients in China accounted for 10%-12% of the total number of TB patients
95 in the world, ranking second in the world(Glaziou et al. 2018; Zhang et al. 2016).People in Gansu
96 Province of China have a high incidence of tuberculosis and are relatively delayed in seeking
97 medical care(Zhang et al. 2016).The presentation of tuberculosis is increasingly
98 atypical.Unfortunately, the prevalence of drug-resistant strains of TB is increasing(Lee et al.
99 2015). The main treatment of epididymal tuberculosis is early anti-tuberculosis treatment.
100 However, since most of the patients with epididymal tuberculosis in Gansu are in the terminal
101 stage, surgical treatment combined with chemotherapy has been the best treatment modality for

102 this type of patients.

103 Reproductive system tuberculosis can occur in any age, mainly in men 30 to 50 years old.Due
104 to the long incubation period,it is not common in children. The most commonly involved organ is
105 the epididymis, followed by the seminal vesicle, prostate, testis, and vas deferens(Yadav et al.
106 2017).Isolated epididymal tuberculosis is very rare(Gueye et al. 1998).One new study indicates
107 that isolated epididymal tuberculosis may be the first or only manifestation of early genitourinary
108 tuberculosis(Viswaroop et al. 2005). Similarly,in our patient cohort,there were 39 cases (82.9%)
109 of isolated epididymal tuberculosis.

110 The pathogenesis of epididymal tuberculosis includes blood-borne transmission and
111 transurethral reflux of *Mycobacterium tuberculosis* caused by factors such as trauma, alcohol
112 abuse and excessive sexual activity(Tzvetkov & Tzvetkova 2006).Epididymal tuberculosis lesions
113 first appear in the tail of the epididymis, owing to its rich blood supply and to retrograde infection
114 from the vas deferens.The lesions of epididymal tuberculosis gradually invade the body to the
115 head, finally affecting the entire epididymis. In severe cases, the testis can be involved(Chung et
116 al. 1997). In this group, 21 patients (44.7%) with epididymal tuberculosis invading the testis
117 underwent radical resection of the testicle. In our study, the main cause of the patient's visit was
118 painless mass of the epididymis, which is consistent with previous studies(Kho & Chan 2012).
119 However,the proportion of patient with scrotal pain is higher, mainly because the patients included
120 in this study all had advanced epididymal tuberculosis or involvement of the testis or scrotum.

121 The gold standard for diagnosing tuberculosis is the isolation and culture of *Mycobacterium*
122 *tuberculosis*.In cases of suspected genitourinary tuberculosis, we usually look for *M. tuberculosis*
123 in the urine or tissue.Traditionally, the appearance of so-called sterile pyuria on microscopic
124 urinalysis is considered to be a typical manifestation of urogenital involvement. In our patient
125 cohort, leukocytes in urine were present microscopically (50%) or grossly in a majority of cases
126 (50% and 10%, respectively).Hematuria and acidic urine have been associated with urinary
127 tuberculosis, but they are nonspecific findings.Color Doppler ultrasound is the first choice for
128 imaging analysis of epididymal tuberculosis(Viswaroop et al. 2005). CT and MR have little value
129 in diagnosing epididymal tuberculosis; they are mainly used to diagnose tuberculosis in lung and
130 kidney and provide support for the diagnosis of epididymal tuberculosis. Epididymal fine needle
131 biopsy is a good method for the diagnosis of epididymal tuberculosis.

132 Tuberculous epididymitis can be the only manifestation of genitourinary tuberculosis.
133 Therefore, even in the absence of clinical and laboratory markers of renal and urologic
134 tuberculosis,all men with identifed epididymal lesions should undergo a fine needle aspiration
135 biopsy.Kim(Kim et al. 1993)suggests that epididymal tuberculosis can often be diagnosed by B-

136 ultrasound biopsy, which supports the above conclusions. Polymerase chain reaction has been an
137 important method for diagnosme.Combined with pathological biopsy,it can improve the diagnosis
138 rating epididymal tuberculosis in recent years(Chawla et al. 2012). It has the characteristics of high
139 sensitivity,high specificity, and short turnaround tie. However, at present, the diagnosis of simple
140 epididymal tuberculosis is difficult, and there is no preoperative diagnostic method with high
141 sensitivity and specificity. The clinical diagnosis of scrotal abscess and ulceration is not difficult.
142 It is often possible to make a clear diagnosis by examining for acid-fast bacilli in samples of the
143 ruptured tissue through pus or secretion smears.

144   The differential diagnosis of epididymal tuberculosis includes bacterial epididymitis,
145 epididymal sperm granuloma, epididymal tumor, and other diseases. Patients with bacterial
146 epididymitis often have testicular-epididymis pain, and scrotal swelling and heat. Features include
147 a shorter course of illness, and symptoms are generally relieved after antibiotic treatment.
148 Carl(Carl & Stark 1997) reported that epididymal tuberculosis should be highly suspected when
149 patients have persistent or repeated epididymitis episodes and symptoms cannot be controlled after
150 adequate antibiotic treatment.

151   Epididymal sperm granuloma mainly occurs in the head of the epididymis, characterized by a
152 smooth solid mass, and antibiotics and anti-tuberculosis treatment are ineffective. Epididymal
153 tumors are rare, accounting for about 0.9% of male reproductive system tumors. Most tumors occur
154 during periods of sexual activity in men between 20 and 40 years of age. The disease is
155 characterized by slow growth, large volume, and no tenderness. CT helps to confirm the diagnosis.
156   Epididymal tuberculosis, like other tuberculosis diseases, requires early, regular, full-course,
157 moderate, combined anti-tuberculosis treatment. The drug treatment method uses 3 to 4 anti-
158 tuberculosis drugs for 6 to 9 months(Peloquin 2014). Surgical treatment is necessary if there is no
159 response to drug treatment or in cases of cold abscess formation. Because the early symptoms of
160 epididymal tuberculosis are not obvious, abscesses or involvement of surrounding tissues such as
161 the testicles have often developed at the time of treatment, so most patients need surgery. In 28
162 cases in our patient cohort (59.6%) presenting as a testicular painless mass, the epididymal-testis
163 border was unclear, or sinus formation was found, suggesting that the surrounding tissues were
164 invaded. Although surgical resection is effective, patients still need regular anti-tuberculosis
165 chemotherapy for 3 to 6 months after surgery and close follow-up.

166 **Conclusion:**epididymal tuberculosis is easy to diagnose in patients with a history of tuberculosis.
167 However, in isolated epididymal tuberculosis, early symptoms are not obvious and cases are
168 typically advanced at the time of diagnosis. There are obvious symptoms and signs such as
169 epididymal enlargement, falling pain and bead-like changes. Epididymal tuberculosis has invaded

170 surrounding tissue by the time it is discovered. Surgical resection combined with preoperative and
171 postoperative chemotherapy is an effective treatment approach. When epididymal tuberculosis
172 manifests bead-like changes, testicular involvement, or sinus formation, good results can be
173 achieved with definitive epididymal-testicular resection. This experiment involved a relatively
174 small number of cases, and the patients did not undergo needle biopsy. Therefore, further research
175 is needed to further characterize this disease and refine the treatment.
176

177 **Reference**

178 Carl P, and Stark L. 1997. Indications for Surgical Management of Genitourinary Tuberculosis. *World Journal of*
179   *Surgery* 21:505-510.

180 Chawla A, Chawla K, Reddy S, Arora N, Bairy I, Rao S, Hegde P, and Thomas J. 2012. Can Tissue PCR Augment the
181   Diagnostic Accuracy in Genitourinary Tract Tuberculosis? *Urologia Internationalis* 88:34-38.

182 Chung JJ, Kim MJ, Lee T, Yoo HS, and Lee JT. 1997. Sonographic findings in tuberculous epididymitis and epididymo-
183   orchitis. *J Clin Ultrasound* 25:390-394.

184 Glaziou P, Floyd K, and Raviglione MC. 2018. Global Epidemiology of Tuberculosis. *Semin Respir Crit Care Med* 39:271-
185   285. 10.1055/s-0038-1651492

186 Gueye SM, Ba M, Sylla C, Ndoye A, Fall A, Diaw J, and Mensah A. 1998. Epididymal manifestations of urogenital
187   tuberculosis. *Progrès En Urologie Journal De Lassociation Française Durologie Et De La Société Française*
188   *Durologie* 8:240.

189 Kho KS, and Chan PH. 2012. Isolated tuberculous epididymitis presenting as a painless scrotal tumor. *Journal of the*
190   *Chinese Medical Association Jcma* 75:292-295.

191 Kim SH, Pollack HM, Cho KS, Pollack MS, and Han MC. 1993. Tuberculous Epididymitis and Epididymo-Orchitis:
192   Sonographic Findings. *J Urol* 150:81-84.

193 Kulchavenya E, Kim C-S, Bulanova O, and Zhukova I. 2012. Male genital tuberculosis: epidemiology and diagnostic.
194   *World Journal of Urology* 30:15-21.

195 Lee HY, Lee J, Lee YS, Kim MY, Lee HK, Lee YM, Shin JH, and Ko Y. 2015. Drug-resistance pattern of Mycobacterium
196   tuberculosis strains from patients with pulmonary and extrapulmonary tuberculosis during 2006 to 2013 in
197   a Korean tertiary medical center. *Korean J Intern Med* 30:325-334. 10.3904/kjim.2015.30.3.325

198 Peloquin DCA. 2014. Therapeutic Drug Monitoring in the Treatment of Tuberculosis. *Drugs* 74:839-854.

199   Surati KN, Suthar KD, and Shah JK. 2012. Isolated Tuberculous Epididymo–Orchitis: A Rare and Instructive Case
200   Report. *Southeast Asian Journal of Case Report & Review*.

201   Tzvetkov D, and Tzvetkova P. 2006. TUBERCULOSIS OF MALE GENITAL SYSTEM – MYTH OR REALITY IN 21ST CENTURY.
202   *Archives of Andrology* 52:375-381.

203   Viswaroop BS, Kekre N, and Gopalakrishnan G. 2005. Isolated tuberculous epididymitis: a review of forty cases.
204   *Journal of Postgraduate Medicine* 51:109.

205   Yadav S, Singh P, Hemal A, and Kumar R. 2017. Genital tuberculosis: current status of diagnosis and management.
206   *Translational Andrology & Urology* 6:222-233.

207   Zhang S, Luo Y, Wang C, Xiong H, Fu SJ, and Yang L. 2016. Open surgery versus retroperitoneal laparoscopic
208   nephrectomy for renal tuberculosis: a retrospective study of 120 patients. *Peerj* 4:e2708.

209

The clinical manifestations and diagnosis in 47 patients with epididymal Tuberculosis

	number	percentage(%)
Location		
left	15	31.90
right	22	46.80
bilateral	10	21.30
Symptoms		
painless swelling	21	44.70
scrotal drop pain	21	44.70
urinary tract irritation	4	8.50
scrotal skin ulceration	1	2.10
Systemic symptoms		
yes	6	12.80
no	41	84.20
Physical examination		
epididymal beaded enlargement	12	25.50
testicular mass	1	2.10
scrotal tenderness	7	14.90
ill-defined epididymal testicular border	21	44.70
sinus formation	6	12.80
History of tuberculosis		
pulmonary tuberculosis	3	0.06
renal tuberculosis	4	0.08
prostate tuberculosis	1	0.02
no	39	0.84
Preoperative diagnosis		
tuberculosis	41	87.20
tumors	3	6.40
masses	3	6.40

Association between surgical methods and physical examination

	total	epididymal resection	epididymis-testicular resection
ill-defined epididymal testicular border	21	16(76.2%)	5(23.8%)
epididymal beaded enlargement	12	10(83.3%)	2(16.7%)
scrotal tenderness	7	7(100%)	0
sinus formation	6	3(100%)	3(100%)
testicular mass	1	1(100%)	0

Figure 1

Microscopy images of caseous necrosis
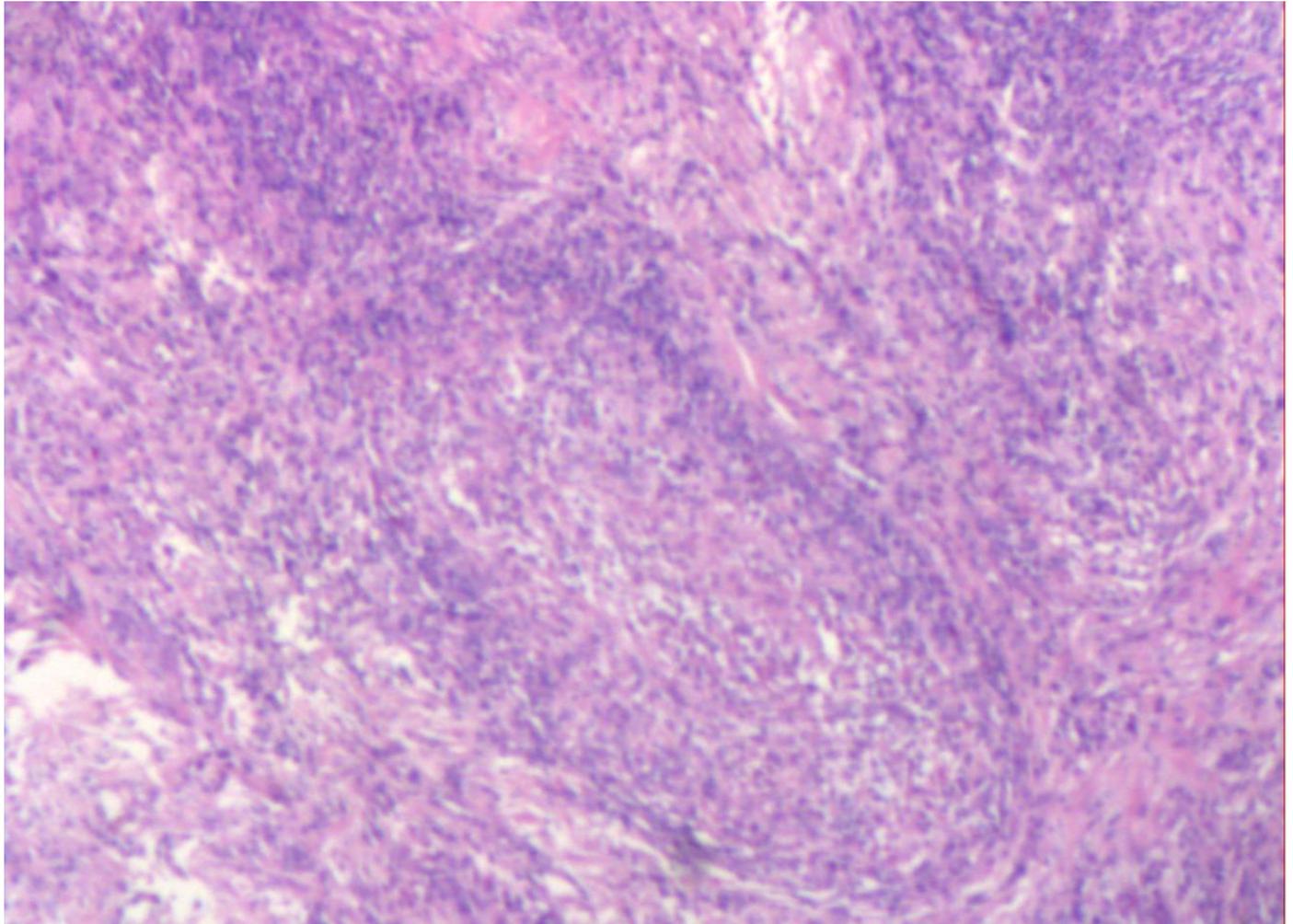
Figure 2

Microscopy images of caseous necrosis